Peer Review File
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Comment 1:

The bile acid phospholipid conjugate ursodeoxycholate 4 lysophoshatidylethanolamide acts by binding to calcium independent membrane 5 phospholipase A2 type beta

The authors have investigated the putative affinity between the bile acid conjugate UDCA-LPE and phospholipase iPLA2-beta. In the paper, the authors suggest an interaction between UDCA-LPE and iPLA2-beta that can have implication of hepatic liver fat.
Overall, this paper is of interest to the research filed of lipids as well as for diabetes research. Major limitation is the paper structure, the results section includes text that belongs in the method, introduction or discussion part, which makes it hard to read.
Reply 1: *Many thanks for reading and evaluating our paper. We are grateful for your comments. Following your advice, we have made some changes that are marked in red letter within the text.*

Comment 2:

Introduction:
In the introduction the authors state that the LPC:PC ratio is indicative of iPLA2 activity according to the reference Puri et al 2007. However, never in this paper this is supported. Please provide a new reference or remove the statement.
Reply 2: *We fully agree with your concern. We have replaced this reference with a review by Law and colleagues (Int. J. Mol. Sci. 2019;20:1149), in which aspects of lysophosphatidylcholine metabolism in human diseases are summarized. In the abstract and text of this review it is stated "LPC is mainly derived from the turnover of phosphatidylcholine in the circulation by phospholipase A2 (PLA2)."*

Comment 3:

The authors do not fully describe and motivate the link between PLA2-activity and hepatic lipid content. Please add this into the introduction. A suggestion is to move the statement in the method section on row 181-182 to the introduction.
The authors state three PLA-isoforms alpha, beta and gamma, but the authors fail to mention the complexity of different PLA2's related to their location, i.e., cytosolic, intracellular and secretary PLA2's. Please add references to support these statements.
Reply 3: *We are grateful for this suggestion. We have added a short statement between PLA2 activity and hepatic lipid content in the introduction section and added some short sentences on the complexity of phospholipases A2.*

Comment 4:

Methods: No statistical evaluation strategy of the dicking results is presented in the method section. The docking procedure is sparsely described. Part of the result section could be moved to the method section.
Reply 4: *As suggested we have moved some part of the result section to the method*

section and added two more sentences about the docking methodology we used for predicting. As stated in the Method section, the docking experiments were done with AutoDock4. The algorithms in this program calculate potential interactions by predicting bound conformations and binding energies of ligands such as pyrrophenone or UDCA-LPE with macromolecular targets such as iPLA2β. After incorporation of all coordinates, the program automatically calculates the best docking sites without the need of sophisticated statistical evaluation. In the original paper that describes AutoDock4, the program has been calibrated on a set of 188 diverse protein-ligand complexes of known structure and binding energy, showing a rather low standard error in prediction of binding free energy in cross-validation studies. We have added some short comment on AutoDock4 in the Method part of our revised paper.

Comment 5:

Results:
It is not clear why the authors used a cPLA2alpha (cytosolic)-inhibitor to evaluate iPLA2-beta (intracellular). Are the two lipases structurally similar? If so state that please.

Reply 5: *That is correct. The two lipases are structurally similar and there is already a lot of information available how the cPLA2alpha inhibitor binds to cPLA2alpha. Therefore, this interaction was taken as a template in our docking analysis. However, we have added some more critical comments at the end of our paper (see also Reply on Comment 6) to highlight this issue.*

Comment 6:

Discussion
It is not clear how specific these results are. What are the limitations and possible confounding of the obtained results/study design?

Reply 6: *According to your advice, we have added two more critical sentences in which we discuss the limitations of our study.*